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SMITH, GAMBRELL & RUSSELL, LLP
ATTORNEYS AT LAW
SUITE 800
1850 M STREET, N.W.
WASHINGTON, DC 20036

EXAMINER	
KANTAMNENI, SHOBHA	
ART UNIT	**PAPER NUMBER**
1617	

DATE MAILED: 03/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/881,213	SANDBERG ET AL.	
	Examiner	Art Unit	
	Shobha Kantamneni	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 December 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,7,9-11 and 22-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *NONE* is/are allowed.

6)☒ Claim(s) *1,3,4,7, 9-11, 22-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The Amendment received on 12/05/2005, wherein claims 1, 3, 4, 7, 9, 10, 11, 22, 24 have been amended, and claims 2, 5, and 21 have been cancelled.

Applicant's amendment to claims 10 and 11 for minor informalities overcomes the objection made in the previous office action dated 06/03/2005.

Applicant's amendment by deleting the term "derivatives or fragments thereof having essentially the same binding function to biotin as avidin or streptavidin", and deleting the word "functionality" in claim 1, and amending claim 11 overcomes the rejection of claims 1, and 11 under 35 U.S.C. 112, second paragraph, as being indefinite.

Applicant's amendment to recite the trifunctional crosslink moiety as an aromatic compound with 1, 3, 5 substitution overcomes the rejection of Claim 1 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for specific trifunctional crosslinking moieties, does not reasonably provide enablement for all moieties which would fall within the scope of the genus described by trifunctional crosslinking moieties.

Applicant's amendment has overcome the rejection of Claim 1-5, 7, 9, and 21-24 under 35 U.S.C. 112, first paragraph because the specification, while being enabling for specific toxin binding moieties, such as biotin, does not reasonably provide enablement for any toxic binding moiety.

Applicant's cancellation of claims 2, 5, and 21 overcomes the rejection of claims 2, 5, and 21 only under 35 U.S.C. 103(a) as being unpatentable over Stayton et al.

(USPN 6413934) in view of both Wilbur et al. (WO 97/291 14) and Ribi et al. (USPN 5491097). See under response to arguments.

Claims 1, 3, 4, 7, 9-11, and 22-24 are examined herein.

Applicant's amendment necessitated the new ground(s) of rejection presented in this office action.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3, 4, 7, 9-11 and 22-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stayton et al. (USPN 6413934) in view of both Wilbur et al. (WO 97/291 14) and Ribi et al. (USPN 5491097), rejection of record.

Stayton et al. teaches streptavidin derivatives containing a biotin binding domain and a specific binding domain (i.e. a secondary functional domain), which binds a compound of interest, as useful for diagnostic purposes in devices such as vascular devices. The streptavidin derivatives are taught to be immobilized on a biotinylated substrate (via the biotin binding domain). The specific binding domain of the streptavidin derivative then captures the compound of interest. See col. 10, lines 23-67. Stayton et al. teaches that streptavidin derivatives were used, specifically, because they are known

to be a powerful biotin-binding protein and that the ability to bind biotin tightly makes the biotin-streptavidin binding affinity essentially irreversible under normal physiological conditions (col. 1 , lines 18-33*, col. 3, lines 34-40). Stayton et al. does not disclose a method using the compounds claimed, an extracorporeal device or that the biotin binding domain consists of avidin or streptavidin, specifically.

Wilbur et al. teaches the biotin containing compounds as instantly claimed (see, e.g., pp. 29-34). The compounds are taught to include a functional moiety useful for diagnostic purposes (Abstract). Linkers comprising hydroxyl functionalities are taught (p. 17, lines 20-23). Biotin sulfones are taught (p. 6, 3). The compounds are taught to comprise at least a biotin moiety and another moiety, which may be another biotin moiety, a reactive moiety or a functional moiety (p. 5, lines 18-20., p. 9, lines 14-24). For the trifunctional cross-linking moiety 5-amino-1, 3-dicarboxybenzene, see, e.g., p. 18, 23. For the linker 4,7, 10-trioxa-13-tridecanediamine and biotin as the binder, see, e.g., p. 31, **48**. It is also taught that in the trimeric biotin compound comprising water soluble linker, the biotin moieities are at a distance that permit two of the biotin molecules to bind with one avidin or streptavidin. See page 31.

Ribi et al. teaches that biotin binding surfaces are known to be comprised of streptavidin and avidin (col. 7, lines 23-29).

It would have been obvious to one of ordinary skill in the art to replace the steps of (1) biotinylating the biotin binding domain of a diagnostic device and (2) binding the streptavidin derivative to the biotinylated substrate of Stayton et al. with the single step of biotinylating the biotin binding domain of a device with the biotin compounds of Wilbur

et al. because (1) Stayton et al. and Wilbur et al. are both directed to inventions wherein biotin is connected to a second functional moiety', (2) the goal of Stayton et al. is to transform a biotin binding surface into a functionalized surface capable of capturing target compounds other than biotin; and (3) Wilbur et al. teaches a compound capable of binding to a biotin binding surface while also leaving a functional moiety free. One would have been motivated to substitute the biotin-streptavidin complex of Stayton et al. with the compounds of Wilbur et al. because, as is shown by the teachings of Stayton et al. and Wilbur et al., the two are known in the art to be interchangeable agents comprising biotin on one side and a functionalized moiety on the other. Furthermore, one would have been motivated to substitute the complex of Stayton et al. with the compounds of Wilbur et al. because Stayton et al. teaches that the advantage of using streptavidin derivatives on a biotinlylated substrate is that streptavidin is known to have a strong affinity for biotin. Accordingly, it would be of a greater advantage to utilize a system wherein the interaction between the biotin and the functionalize moiety is actually achieved via covalent bonding. Finally, one would have been motivated to substitute the complex of Stayton et al. with the compounds of Wilbur et al. because doing so would reduce the number of steps required to functionalize the surface in the manner desired.

It would have been obvious to one of ordinary skill in the art to utilize a device wherein the biotin binding surface containing streptavidin or avidin as the biotin binding molecules because Ribi et al. teaches that it is known in the art to prepare biotin binding surfaces in such a manner. One would have been motivated to specifically utilize

streptavidin or avidin as the biotin binding molecules because Stayton et al. teaches a biotin binding domain, generally, and a biotin binding domain comprising streptavidin or avidin molecules is within the scope of the genus taught by Stayton et al.

It is noted that the skilled artisan would recognize that a diagnostic device must, necessarily, be either extracorporeal or implanted and the skilled artisan would have found it obvious to utilize the method of the combined references in either extracorporeal or implanted devices because Stayton et al. teaches diagnostic devices, generally.

It is further noted that the binding affinity of a molecule is a property of said molecule. Accordingly, since Wilbur et al. teaches the same compounds as instantly claimed, it is Examiner's position that, absent evidence to the contrary, the compounds will have the same binding affinities as instantly claimed, and the compounds taught by Wilbur et al. containing two biotins will be attached to the same avidin or streptavadin. A product and its properties are inseparable. *In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963).

Response to Arguments

Applicant argues that "Stayton teaches nothing regarding the creation of a structural network between avidin/streptavidin and the reagent". This argument is not persuasive because Stayton teaches that biotinylated compounds which are obtained by well known techniques are bound to the biotin binding domain of streptavidin molecule, and thus result in a structural network between avidin/streptavidin.

Applicant's argument that "Wilbur does not teach or suggest a method of conditioning an extracorporeal device or how to establish a structural network between the reagent and the device, which is possible to create with the reagent used in Applicant's claim 1 method." This argument is not persuasive because 1) applicant is arguing against an individual reference when the rejection was based on a combination of references, and Wilbur teaches a method of obtaining a structural network by cross-linking streptavidin with biotinylated compounds such as biotin moiety dimers comprising water soluble linkers, biotin moiety trimers comprising water soluble linkers. (See page 65), and Stayon et al. teaches diagnostic devices generally. Thus, one of ordinary skill in the art at the time of invention would have found it obvious to utilize the method of combined references in either extracorporeal or implanted devices because the diagnostic device must necessarily be either extracorporeal or implanted.

Applicant's argument that "Wilbur teaches biotin compounds which may be monomers as well as dimeric, trimeric or multimeric biotin compounds. In a biotin dimer, it is important that the distance between the two biotin moieties is long enough (more than 15 angstroms) to bind two proteins, but short enough (less than 20 angstroms) that

the two biotins will not bind to the same avidin or streptavidin molecule (see page 29, lines 15-17)." This argument is not persuasive. It is respectfully pointed out that in the claim 1, it is recited that "a and b provide between about 20 angstroms and 60 angstroms between each biotin moiety carboxylate carbon atom when measured in a fully linearized form", and Wilbur also teaches that the distance between each biotin moiety in the biotin trimer is preferably from about 20 angstroms to about 50 angstroms. And further Wilbur teaches linkers within the scope of the linker lengths as claimed herein, and thus meets the instant claims. See page 31, Example 48 which reads on instant claims with biotin as toxin binding moiety.

Applicant's argument that "There is no clear link or guidance between the cited references, and no motivation, reason or suggestion for one skilled in the art to combine the references to arrive at Applicants claimed method. Specifically, none of the cited references addresses questions or solves problems that are relevant to arrive at the present invention without undue burden." This argument is not persuasive because as discussed above one of ordinary skill in the art at the time of invention would have been motivated to substitute the complex of Stayton et al. with the compounds of Wilbur et al. because Stayton et al. teaches that the advantage of using streptavidin derivatives on a biotinylated substrate such as streptavidin is known to have a strong affinity for biotin. Accordingly, it would be of a greater advantage to utilize a system wherein the interaction between the biotin and the functionalize moiety is actually achieved via covalent bonding. Finally, one would have been motivated to substitute the complex of

Stayton et al. with the compounds of Wilbur et al. because doing so would reduce the number of steps required to functionalize the surface in the manner desired.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period, will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shobha Kantamneni whose telephone number is 571-272-2930. The examiner can normally be reached on Monday-Friday, 8am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Shobha Kantamneni, Ph.D
Patent Examiner
Art Unit : 1617

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER